AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

1. (currently amended) A ~~drug~~ method for improving glucose intolerance comprising administering to a subject in need thereof a glucose intolerance improving amount of a chymase inhibitor ~~as an active ingredient~~.

2. (currently amended) A ~~preventive drug and/or therapeutic drug~~ method for prevention and/or treatment of diseases caused by glucose intolerance comprising administering to a subject in need thereof a pharmaceutically effective amount of a chymase inhibitor ~~as an active ingredient~~.

3. (currently amended) ~~A preventive and/or therapeutic drug~~ The method for prevention and/or treatment according to claim 2 wherein the diseases caused by glucose intolerance are diabetes and/or diabetes complications.

4. (currently amended) ~~A preventive and/or therapeutic drug~~ The method for prevention and/or treatment according to claim 3 wherein the diabetes complications are diabetic nephropathy, diabetic retinopathy, diabetic peripheral neuropathy, hyperinsulinism, insulin resistance syndrome, arteriosclerosis, acute coronary syndrome, arteriosclerosis obliterans,

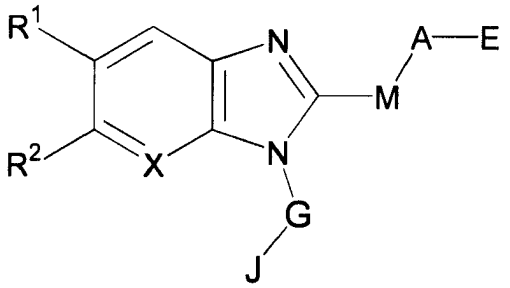
angitis, stroke, hypertension, renal insufficiency, nephropathy, nephritis, renal artery aneurysm, renal infarction or obesity.

5. (currently amended) ~~A preventive and/or therapeutic drug~~ The method for prevention and/or treatment according to claim 3 wherein the diabetes complications are diabetic nephropathy, diabetic retinopathy or diabetic peripheral neuropathy.

6. (canceled).

7. (currently amended) ~~A drug described in~~ The method for prevention and/or treatment according to any one of claims ~~1–6~~2 - 5 further comprising administering an ACE inhibitor.

8. (currently amended) ~~A drug described according to any of claims 1–7~~ The method for prevention and/or treatment according to any one of claims 2-5 wherein the chymase inhibitor is the compound represented by formula (I):



(I)

[wherein R^1 and R^2 simultaneously or each independently represent hydrogen, halogen, trihalomethyl, cyano, hydroxyl, C_1–C_4 alkyl or C_1–C_4 alkoxy, or R^1 and R^2 taken together

represent –O–CH_2–O–, –O–CH_2CH_2–O– or –$CH_2CH_2CH_2$–, (wherein the carbon atoms may be optionally substituted by one or more C_1–C_4 alkyl);

A represents substituted or unsubstituted straight, cyclic or branched C_1–C_7 alkylene or alkenylene, which may be interrupted by one or more of atoms or groups selected from –O–, –S–, $–SO_2–$ and $–NR^3–$ (wherein R^3 represents hydrogen or straight or branched C_1–C_6 alkyl), the substituents on these groups being selected from halogen, hydroxyl, nitro, cyano, straight or branched C_1–C_6 alkyl, straight or branched C_1–C_6 alkoxy (including cases wherein the neighboring two form an acetal), straight or branched C_1–C_6 alkylthio, straight or branched C_1–C_6 alkylsulfonyl, straight or branched C_1–C_6 acyl, straight or branched C_1–C_6 acylamino, trihalomethyl, trihalomethoxy, phenyl, oxo or phenoxy optionally substituted with one or more halogen atoms, wherein one or more of these substituents may each independently be present at any position in the alkylene or alkenylene, except for the case wherein M represents a single bond and the carbon atom of A directly bonded to M is substituted with a hydroxyl and a phenyl at the same time;

E represents $–COOR^3$, $–SO_3R^3$, $–CONHR^3$, $–SO_2NHR^3$, tetrazol-5-yl, 5-oxo-1,2,4-oxadiazol-3-yl or 5-oxo-1,2,4-thaidiazol-3-yl, (wherein R^3 is as defined above);

G represents substituted or unsubstituted straight or branched C_1–C_6 alkylene, which may be interrupted by one or more of atoms or groups selected from –O–, –S–, $–SO_2–$ and $–NR^3–$ (wherein R^3 is as defined above, provided that either of these atoms or groups is not directly attached to the benzimidazole ring), the substituents on the said alkylene being selected from halogen, hydroxyl, nitro, cyano, straight or branched C_1–C_6 alkyl, straight or branched C_1–C_6

alkoxy (including cases wherein neighboring two form an acetal), trihalomethyl, trihalomethoxy, phenyl or oxo;

M represents a single bond or $-S(O)_m-$, wherein m is an integer ranging from 0 to 2;

J represents substituted or unsubstituted C_4-C_{10} heteroaryl (one or more heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur in the ring), except for imidazole or unsubstituted pyridine ring, the substituents on the said heteroaryl are halogen, hydroxyl, nitro, cyano, straight or branched C_1–C_6 alkyl, straight or branched C_1–C_6 alkoxy (including cases wherein neighboring two form an acetal), straight or branched C_1–C_6 alkylthio, straight or branched C_1–C_6 alkylsulfonyl, straight or branched C_1–C_6 acyl, straight or branched C_1–C_6 acylamino, substituted or unsubstituted anilido, trihalomethyl, trihalomethoxy, phenyl, oxo, $COOR^3$ or phenoxy optionally substituted with one or more halogen atoms, wherein one or more of these substituents may each independently be present at any position in the ring; and

X represents –CH= or nitrogen].

9. (currently amended) ~~A drug~~ The method for prevention and/or treatment according to claim 8 wherein, in formula (I), R^1 and R^2 are simultaniously or each independently hydrogen, C_1–C_4 alkyl, C_1–C_4 alkoxy, halogen or cyano;

A is n-propylene;

E is –COOH;

G is methylene;

M is –S–;

J is substituted or unsubstituted benzothienyl or indolyl (wherein the substituent is halogen, hydroxyl, nitro, cyano, straight or branched C_1–C_6 alkyl, straight or branched C_1–C_6 alkoxy (including cases wherein neighboring two form an acetal), straight or branched C_1–C_6 alkylthio, straight or branched C_1–C_6 alkylsulfonyl, straight or branched C_1–C_6 acyl, straight or branched C_1–C_6 acylamino, substituted or unsubstituted anilido, trihalomethyl, trihalomethoxy, phenyl, oxo, $COOR^3$ or phenoxy optionally substituted with one or more halogen atoms, wherein one or more of these substituents may each independently be present at any position in the ring); and X is –CH=.

10. (currently amended) ~~A drug~~ The method for prevention and/or treatment according to claim ~~8 or 9~~ wherein R^1 and R^2 are simultaneously or each independently hydrogen, C_1–C_4 alkyl or C_1–C_4 alkoxy.

11. (currently amended) ~~A drug~~ The method for prevention and/or treatment according to claim 10 wherein R^1 and R^2 are simultaneously or each independently hydrogen, methyl or methoxy.

12. (currently amended) ~~A drug according to any of claims 8–11~~ The method for prevention and/or treatment according to claim 8 wherein J is benzothienyl.

13. (currently amended) ~~A drug according to any of claims 8–12~~ The method for prevention and/or treatment according to claim 8 wherein the substituent on J is halogen, cyano, straight or

branched C_1–C_4 alkyl, straight or branched C_1–C_4 alkoxy (including cases wherein neighboring two form an acetal) or trihalomethyl.

14. (currently amended) ~~A drug~~ The method for prevention and/or treatment according to claim 13 wherein the substituent on J is F, Cl, cyano, methyl, methoxy or trifluoromethyl.

15. (currently amended) ~~A drug~~ The method for prevention and/or treatment according to claim 14 wherein the substituent on J is methyl.

16. (currently amended) ~~A drug according to any of claims 1–7~~ The method for prevention and/or treatment according to any one of claims 2-5 wherein the chymase inhibitor is 4-(1-((3-indolyl)methyl)benzimidazol-2-ylthio)butanoic acid, 4-(1-((3-benzo[b]thienyl)methyl)-5-methoxybenzimidazol-2-ylthio)butanoic acid, 4-(1-((5-methylbenzo[b]thiophen-3-yl)methyl)-5-methoxybenzimidazol-2-ylthio)butanoic acid, 4-(1-((4-methylbenzo[b]thiophen-3-yl)methyl)-5-methoxybenzimidazol-2-ylthio)butanoic acid,
4-(1-((3-benzo[b]thienyl)methyl)-5-cyanobenzimidazol-2-ylthio)butanoic acid, 4-(1-((5-methylbenzo[b]thiophen-3-yl)methyl)-6-methoxybenzimidazol-2-ylthio)butanoic acid, 4-(1-((4-methylbenzo[b]thiophen-3-yl)methyl)-6-methoxybenzimidazol-2-ylthio)butanoic acid,
4-(1-((1,5-dimethylindol-3-yl)methyl)benzimidazol-2-ylthio)butanoic acid, 4-(1-((1-methyl-4-chloroindol-3-yl)methyl)benzimidazol-2-ylthio)butanoic acid, 4-(1-((1-methyl-4-fluoroindol-3-yl)methyl)benzimidazol-2-ylthio)butanoic acid, 4-(1-((5-chlorobenzo[b]thiophen-3-yl)methyl)benzimidazol-2-ylthio)butanoic acid, 4-(1-((5-methylbenzo[b]thiophen-3-

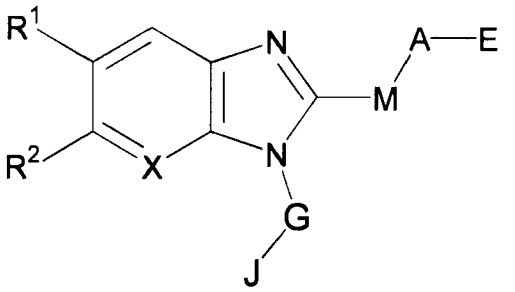
yl)methyl)benzimidazol-2-ylthio)butanoic acid, 4-(1-((4-methylbenzo[b]thiophen-3-yl)methyl)benzimidazol-2-ylthio)butanoic acid, 4-(1-((4-chlorobenzo[b]thiophen-3-yl)methyl)benzimidazol-2-ylthio)butanoic acid, 4-(1-((4,6-dimethylbenzo[b]thiophen-3-yl)methyl)benzimidazol-2-ylthio)butanoic acid, 4-(1-((1-methylindol-3-yl)methyl)-5,6-dimethylbenzimidazol-2-ylthio)butanoic acid, 4-(1-((1,4-dimethylindol-3-yl)methyl)-5,6-dimethylbenzimidazol-2-ylthio)butanoic acid, 4-(1-((1-methyl-4-chloroindol-3-yl)methyl)-5,6-dimethylbenzimidazol-2-ylthio)butanoic acid, 4-(1-((benzo[b]thiophen-3-yl)methyl)-5,6-dimethylbenzimidazol-2-ylthio)butanoic acid, 4-(1-((5-chlorobenzo[b]thiophen-3-yl)methyl)-5,6-dimethylbenzimidazol-2-ylthio)butanoic acid, 4-(1-((5-methylbenzo[b]thiophen-3-yl)methyl)-5,6-dimethylbenzimidazol-2-ylthio)butanoic acid, 4-(1-((4-methylbenzo[b]thiophen-3-yl)methyl)-5,6-dimethylbenzimidazol-2-ylthio)butanoic acid, 4-(1-((1,4-dimethylindol-3-yl)methyl)-5,6-dichlorobenzimidazol-2-ylthio)butanoic acid, 4-(1-((benzo[b]thiophen-3-yl)methyl)-5,6-dichlorobenzimidazol-2-ylthio)butanoic acid, 4-(1-((benzo[b]thiophen-3-yl)methyl)benzimidazol-2-ylthio)butanoic acid, 4-(1-((benzo[b]thiophen-3-yl)methyl)-5-methylbenzimidazol-2-ylthio)butanoic acid, 4-(1-((benzo[b]thiophen-3-yl)methyl)-6-methylbenzimidazol-2-ylthio)butanoic acid, 4-(1-((1,4-dimethylindol-3-yl)methyl)benzimidazol-2-ylthio)butanoic acid, 4-(1-((1,4-dimethylindol-3-yl)methyl)-5-methoxybenzimidazol-2-ylthio)butanoic acid or 4-(1-((1-methyl-4-chloroindol-3-yl)methyl)-5-methoxybenzimidazol-2-ylthio)butanoic acid.

17. (currently amended) ~~A drug according to any of claims 1–7~~ The method for prevention and/or treatment according to claims 2-5 wherein the chymase inhibitor is 4-(1-((4-methylbenzo[b]thiophen-3-yl)methyl)benzimidazol-2ylthio)butanoic acid.

18. - 28. (canceled).

29. (new): The method according to claim 1 further comprising administering an ACE inhibitor.

30. (new): The method according to claim 1 wherein the chymase inhibitor is the compound represented by formula (I):



(I)

[wherein R^1 and R^2 simultaneously or each independently represent hydrogen, halogen, trihalomethyl, cyano, hydroxyl, C_1–C_4 alkyl or C_1–C_4 alkoxy, or R^1 and R^2 taken together represent –O–CH_2–O–, –O–CH_2CH_2–O– or –$CH_2CH_2CH_2$–, (wherein the carbon atoms may be optionally substituted by one or more C_1–C_4 alkyl);

A represents substituted or unsubstituted straight, cyclic or branched C_1–C_7 alkylene or alkenylene, which may be interrupted by one or more of atoms or groups selected from –O–, –S–, –SO_2– and –NR^3– (wherein R^3 represents hydrogen or straight or branched C_1–C_6 alkyl), the

substituents on these groups being selected from halogen, hydroxyl, nitro, cyano, straight or branched C_1–C_6 alkyl, straight or branched C_1–C_6 alkoxy (including cases wherein the neighboring two form an acetal), straight or branched C_1–C_6 alkylthio, straight or branched C_1–C_6 alkylsulfonyl, straight or branched C_1–C_6 acyl, straight or branched C_1–C_6 acylamino, trihalomethyl, trihalomethoxy, phenyl, oxo or phenoxy optionally substituted with one or more halogen atoms, wherein one or more of these substituents may each independently be present at any position in the alkylene or alkenylene, except for the case wherein M represents a single bond and the carbon atom of A directly bonded to M is substituted with a hydroxyl and a phenyl at the same time;

E represents $-COOR^3$, $-SO_3R^3$, $-CONHR^3$, $-SO_2NHR^3$, tetrazol-5-yl, 5-oxo-1,2,4-oxadiazol-3-yl or 5-oxo-1,2,4-thaidiazol-3-yl, (wherein R^3 is as defined above);

G represents substituted or unsubstituted straight or branched C_1–C_6 alkylene, which may be interrupted by one or more of atoms or groups selected from –O–, –S–, $-SO_2-$ and $-NR^3-$ (wherein R^3 is as defined above, provided that either of these atoms or groups is not directly attached to the benzimidazole ring), the substituents on the said alkylene being selected from halogen, hydroxyl, nitro, cyano, straight or branched C_1–C_6 alkyl, straight or branched C_1–C_6 alkoxy (including cases wherein neighboring two form an acetal), trihalomethyl, trihalomethoxy, phenyl or oxo;

M represents a single bond or $-S(O)_m-$, wherein m is an integer ranging from 0 to 2;

J represents substituted or unsubstituted C_4-C_{10} heteroaryl (one or more heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur in the ring), except for imidazole or unsubstituted pyridine ring, the substituents on the said heteroaryl are halogen, hydroxyl, nitro,

cyano, straight or branched C_1–C_6 alkyl, straight or branched C_1–C_6 alkoxy (including cases wherein neighboring two form an acetal), straight or branched C_1–C_6 alkylthio, straight or branched C_1–C_6 alkylsulfonyl, straight or branched C_1–C_6 acyl, straight or branched C_1–C_6 acylamino, substituted or unsubstituted anilido, trihalomethyl, trihalomethoxy, phenyl, oxo, $COOR^3$ or phenoxy optionally substituted with one or more halogen atoms, wherein one or more of these substituents may each independently be present at any position in the ring; and

X represents –CH= or nitrogen].

31. (new): The method according to claim 30 wherein, in formula (I), R^1 and R^2 are simultaniously or each independently hydrogen, C_1–C_4 alkyl, C_1–C_4 alkoxy, halogen or cyano;

A is n-propylene;

E is –COOH;

G is methylene;

M is –S–;

J is substituted or unsubstituted benzothienyl or indolyl (wherein the substituent is halogen, hydroxyl, nitro, cyano, straight or branched C_1–C_6 alkyl, straight or branched C_1–C_6 alkoxy (including cases wherein neighboring two form an acetal), straight or branched C_1–C_6 alkylthio, straight or branched C_1–C_6 alkylsulfonyl, straight or branched C_1–C_6 acyl, straight or branched C_1–C_6 acylamino, substituted or unsubstituted anilido, trihalomethyl, trihalomethoxy, phenyl, oxo, $COOR^3$ or phenoxy optionally substituted with one or more halogen atoms, wherein one or more of these substituents may each independently be present at any position in the ring); and

X is –CH=.

32. (new): The method according to claim 30 wherein R^1 and R^2 are simultaneously or each independently hydrogen, C_1–C_4 alkyl or C_1–C_4 alkoxy.

33. (new): The method according to claim 32 wherein R^1 and R^2 are simultaneously or each independently hydrogen, methyl or methoxy.

34. (new): The method according to claim 30 wherein J is benzothienyl.

35. (new): The method according to claim 30 wherein the substituent on J is halogen, cyano, straight or branched C_1–C_4 alkyl, straight or branched C_1–C_4 alkoxy (including cases wherein neighboring two form an acetal) or trihalomethyl.

36. (new): The method according to claim 35 wherein the substituent on J is F, Cl, cyano, methyl, methoxy or trifluoromethyl.

37. (new): The method according to claim 36 wherein the substituent on J is methyl.

38. (new): The method according to claim 1 wherein the chymase inhibitor is 4-(1-((3-indolyl)methyl)benzimidazol-2-ylthio)butanoic acid, 4-(1-((3-benzo[b]thienyl)methyl)-5-methoxybenzimidazol-2-ylthio)butanoic acid, 4-(1-((5-methylbenzo[b]thiophen-3-yl)methyl)-5-

methoxybenzimidazol-2-ylthio)butanoic acid, 4-(1-((4-methylbenzo[b]thiophen-3-yl)methyl)-5-methoxybenzimidazol-2-ylthio)butanoic acid, 4-(1-((3-benzo[b]thienyl)methyl)-5-cyanobenzimidazol-2-ylthio)butanoic acid, 4-(1-((5-methylbenzo[b]thiophen-3-yl)methyl)-6-methoxybenzimidazol-2-ylthio)butanoic acid, 4-(1-((4-methylbenzo[b]thiophen-3-yl)methyl)-6-methoxybenzimidazol-2-ylthio)butanoic acid, 4-(1-((1,5-dimethylindol-3-yl)methyl)benzimidazol-2-ylthio)butanoic acid, 4-(1-((1-methyl-4-chloroindol-3-yl)methyl)benzimidazol-2-ylthio)butanoic acid, 4-(1-((1-methyl-4-fluoroindol-3-yl)methyl)benzimidazol-2-ylthio)butanoic acid, 4-(1-((5-chlorobenzo[b]thiophen-3-yl)methyl)benzimidazol-2-ylthio)butanoic acid, 4-(1-((5-methylbenzo[b]thiophen-3-yl)methyl)benzimidazol-2-ylthio)butanoic acid, 4-(1-((4-methylbenzo[b]thiophen-3-yl)methyl)benzimidazol-2-ylthio)butanoic acid, 4-(1-((4-chlorobenzo[b]thiophen-3-yl)methyl)benzimidazol-2-ylthio)butanoic acid, 4-(1-((4,6-dimethylbenzo[b]thiophen-3-yl)methyl)benzimidazol-2-ylthio)butanoic acid, 4-(1-((1-methylindol-3-yl)methyl)-5,6-dimethylbenzimidazol-2-ylthio)butanoic acid, 4-(1-((1,4-dimethylindol-3-yl)methyl)-5,6-dimethylbenzimidazol-2-ylthio)butanoic acid, 4-(1-((1-methyl-4-chloroindol-3-yl)methyl)-5,6-dimethylbenzimidazol-2-ylthio)butanoic acid, 4-(1-((benzo[b]thiophen-3-yl)methyl)-5,6-dimethylbenzimidazol-2-ylthio)butanoic acid, 4-(1-((5-chlorobenzo[b]thiophen-3-yl)methyl)-5,6-dimethylbenzimidazol-2-ylthio)butanoic acid, 4-(1-((5-methylbenzo[b]thiophen-3-yl)methyl)-5,6-dimethylbenzimidazol-2-ylthio)butanoic acid, 4-(1-((4-methylbenzo[b]thiophen-3-yl)methyl)-5,6-dimethylbenzimidazol-2-ylthio)butanoic acid, 4-(1-((1,4-dimethylindol-3-yl)methyl)-5,6-dichlorobenzimidazol-2-ylthio)butanoic acid, 4-(1-((benzo[b]thiophen-3-yl)methyl)-5,6-dichlorobenzimidazol-2-ylthio)butanoic acid, 4-(1-

((benzo[b]thiophen-3-yl)methyl)benzimidazol-2-ylthio)butanoic acid, 4-(1-((benzo[b]thiophen-3-yl)methyl)-5-methylbenzimidazol-2-ylthio)butanoic acid, 4-(1-((benzo[b]thiophen-3-yl)methyl)-6-methylbenzimidazol-2-ylthio)butanoic acid, 4-(1-((1,4-dimethylindol-3-yl)methyl)benzimidazol-2-ylthio)butanoic acid, 4-(1-((1,4-dimethylindol-3-yl)methyl)-5-methoxybenzimidazol-2-ylthio)butanoic acid or 4-(1-((1-methyl-4-chloroindol-3-yl)methyl)-5-methoxybenzimidazol-2-ylthio)butanoic acid.

39. (new): The method according to claim 1 wherein the chymase inhibitor is 4-(1-((4-methylbenzo[b]thiophen-3-yl)methyl)benzimidazol-2ylthio)butanoic acid.